

### REMARKS/ARGUMENTS

Favorable consideration of this application as presently amended and in light of the following discussion is respectfully requested.

Claims 1-48 are pending in the application, with Claims 5, 18, 38, and 46 amended by the present amendment.

In the outstanding Office Action, Claim 29 was objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim; Claims 5-9, 18-22, 38-39 and 46 were rejected under 35 U.S.C. § 112, second paragraph; Claims 13, 26, 31, 44 and 46 were rejected under 35 U.S.C. § 112, second paragraph; Claims 1-3, 13, 28-29, 31, 33-35, 37, 43-44 and 46-48 were rejected under 35 U.S.C. § 102(b) as being anticipated by Dromey; Claims 1-3, 10, 12-13, 15-16, 23, 25-26, 28-31, 33-35, 37, 40, 43-44 and 46-48 were rejected under 35 U.S.C. § 102(b) as being anticipated by Hines; Claims 14, 27, 32 and 45-46 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hines in view of Yates (Analytical Chemistry 1995, 67, 1426-1436); Claims 5, 11, 18, 24, 41-42 and 46 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hines in view of Kwok (Journal of the American Chemical Society, 1973, 95, 4185-4194); Claims 4, 6-9, 17, 19-22, 36, and 38-39 were indicated as containing allowable subject matter.

Applicants gratefully acknowledge the indication of the allowable subject matter.

Applicants traverse the objection to Claim 29 under 37 C.F.R. § 1.75(c). Applicants submit that by reciting that the mass spectra recited in Claim 28 is mass spectra obtained by any one of dissociation and full-scan, Applicants have further limited the mass spectra from mass spectra obtained by means other than dissociation or full-scan.

Applicants have amended Claims 5, 18, 38, and 46 to more clearly describe and distinctly claim Applicants' invention. No new matter is added. Thus, Applicants request

withdrawal of the rejection of Claims 5-9, 18-22, 38-39 and 46 under 35 U.S.C. § 112, second paragraph

Applicants traverse the rejection of Claims 13, 26, 31, 44 and 46 under 35 U.S.C. § 112, second paragraph. Regarding the scope of the terms “automatically specifying said spectral characteristics based on said mass spectra” and “automatically specifying said relationship based on said mass spectra,” Applicants note these limitations are described in Applicants’ disclosure relative to Figures 8 and 9. That is, the two automatic specifying steps are “based on predetermined characteristics of the chemical species being analyzed.”<sup>1</sup> These predetermined characteristics are input by a user.<sup>2</sup> Examples of these predetermined characteristics include product ions at specific  $m/z$  values, neutral or charged losses from singly- or doubly-charged precursors, and ion series or pairs.<sup>3</sup> In other words, the invention is not limited to analysis of mass spectral data obtained by any specific type of chemical compounds (e.g., peptides, oligos) or to ions produced by any particular method (e.g., MALDI, electrospray) or to data from any particular type of mass analyzer (e.g., quadrupole, ion trap, or hybrids). Moreover, the type of mass spectrum may be a full scan spectrum or a tandem mass spectrum. In short, Applicants’ claimed inventions work on *any* mass spectra data acquired on *any* instrument for *any* type of chemical substance. Applicants submit Claims 13, 26, 31, 44 and 46 are definite and respectfully request the outstanding rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

Briefly recapitulating, Claim 1 is directed to a method for mining mass spectra. The method includes a) specifying spectral characteristics of the mass spectra to mine; b) specifying a relationship between the spectral characteristics; c) searching the mass spectra for portions of the mass spectra which match the spectral characteristics based on the relationship; and d) assigning scores to the portions of the mass spectra to indicate a degree of

<sup>1</sup> Specification, page 18, lines 13-15.

<sup>2</sup> Specification, page 18, lines 32-33.

<sup>3</sup> Specification, page 19, lines 1-3 and lines 11-30.

correlation between the portions of the mass spectra and the spectral characteristics.

Applicants' claimed method enables detection of tandem mass spectra data that corresponds to various peptide forms.<sup>4</sup> That is, conventional use of mass spectral data to predict chemical structures and even peptide sequences is well-described in the prior art. However, Applicants' claimed inventions do not predict structures or sequences from MS data. Rather, Applicants' claimed inventions identify data that displays specific characteristics ***defined by the user***. These characteristics include hierarchically defined combinations of loss ions, product ions and ion series. Independent Claims 15, 28, 33, 34, 46, and 47 are directed to alternative embodiments, each identifying data that displays specific characteristics ***defined by the user*** and including hierarchically defined combinations of loss ions, product ions, and ion series.

Dromey discloses the use of a single parameter (series displacement index, SDI) to score spectra. Dromey discloses that this single parameter varies predictably with different chemical classes and that the SDI can be used to identify a chemical class to which an unknown belongs. That is, the method of Dromey takes information from a spectrum of an unknown and then uses the information to search a database. However, Dromey does not disclose or suggest Applicants' claimed sequence of a) specifying spectral characteristics; b) specifying a relationship; c) searching the mass spectra for portions of the mass spectra which match the spectral characteristics based on the relationship; and d) assigning scores. That is, while Applicants' claimed inventions takes information about a compound type (e.g., a loss ion, a product ion, and ion series) and uses it to identify spectra that display the specified characteristic, Dromey discloses a methodology that is the reverse of Applicants' claimed inventions. For at least this reason, Applicants submit the invention recited in independent Claims 1, 15, 28, 33, 34, 46, and 47 patentably define over Dromey and request withdrawal

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<sup>4</sup> Specification, page 2, lines 32-33.

of the rejection of Claims 1-3, 13, 28-29, 31, 33-35, 37, 43-44 and 46-48 under 35 U.S.C. § 102(b).

Hines discloses an algorithm to extract peptide sequences from MS-MS data.

Applicants first note that this approach identifies only ion series in spectra that correspond to sequences. Product ion or loss ion data are not considered or integrated into the algorithm of Hines as recited in Applicants' Claim 5. SALSA integrates all three types of data. More fundamentally, like Dromey, the algorithm of Hines predicts sequences from spectra, whereas Applicants' claimed inventions identify spectra that correspond to sequences or their variant versions. That is, while Applicants' claimed inventions takes information about a compound type (e.g., a loss ion, a product ion, and ion series) and uses it to identify spectra that display the specified characteristic, Hines discloses a methodology that is the reverse of Applicants' claimed inventions (i.e., spectral features are used to derive sequences in Hines, whereas spectral features are used to select data in Applicants' claimed inventions). For at least this reason, Applicants submit the invention recited in independent Claims 1, 15, 28, 33, 34, 46, and 47 patentably define over Hines and request withdrawal of the rejection of 1-3, 10, 12-13, 15-16, 23, 25-26, 28-31, 33-35, 37, 40, 43-44 and 46-48 were rejected under 35 U.S.C. § 102(b).

Applicants have considered the Yates disclosure and submit that Yates does not cure the deficiencies of Hines. Yates discloses the use of uninterpreted spectra to identify matching peptide sequences from databases. Yates identifies modified peptide sequences from spectra *only if the mass and amino acid specificity of the modification can be predicted beforehand*. The masses and sequence specificities of many modifications cannot be predicted beforehand, and Yates searches will not identify peptides bearing these modifications. That is, like Dromey and Hines, the algorithm of Yates predicts sequences from spectra, whereas Applicants' claimed inventions identify spectra that correspond to

sequences or their variant versions. Thus, like Dromey and Hines, the method of Yates is the opposite of that recited in Applicants' independent claims.

Furthermore, Applicants traverse the finding that Yates discloses adjusting parameters of a mass spectrometer in response to a spectral score. Yates discloses that acquisition is triggered by neutral loss scanning, which was already a widely known and widely used technique in mass spectrometry and is not a part of the Yates algorithm. In other words, Yates does not use spectral scores to automatically adjust parameters of the mass spectrometer. Instead, Yates uses the neutral loss scans to trigger the acquisition of MS-MS spectra, which are then searched against a database with the disclosed algorithm to identify peptide sequences.

Applicants have also considered the Kwok reference and submit Kwok does not cure the deficiencies of Hines. Kwok discloses a method for scoring features in mass spectra (including product ions, neutral losses and ion series) and then using the combined scores to search a database of similarly calculated scores for known compounds. Kwok then searches a database to assign structures to the unknown substance. However, like Dromey, Hines, and Yates, Kwok does not disclose or suggest Applicants' claimed sequence of a) specifying spectral characteristics; b) specifying a relationship; c) searching the mass spectra for portions of the mass spectra which match the spectral characteristics based on the relationship; and d) assigning scores. Furthermore, Kwok does not use scores to rank spectra for further interpretation by the user as recited in Applicants' claimed inventions.

Also, as noted previously, the Hines algorithm is based on defined relationships of ion series in peptide MS-MS spectra and does not include neutral losses or product ions as recited in Applicants' Claim 5 and as disclosed in Kwok. Hines failure to disclose relationships of neutral losses or product ions renders the combination of Hines and Kwok incomplete as compared to Applicants' claimed invention. In addition, Applicants traverse the suggestion

that incorporating the features described by Kwok into the de novo sequencing algorithm of Hines would be obvious. Applicants submit the combining of these different types of parameters for peptide sequencing has not been done despite the development of several de novo sequencing programs over the past 10 years. Furthermore, Applicants submit there is no teaching, suggestion, or motivation, either explicitly or implicitly, in either reference to combine the algorithm of Hines with the searching of Kwok to arrive at Applicants' inventions recited in Claims 5, 11, 18, 24, 41-42 and 46. Thus, for each of the previous reasons, Applicants submit the outstanding rejection of Claims 5, 11, 18, 24, 41-42 and 46 under 35 U.S.C. § 103(a) is an impermissible hindsight reconstruction of Applicants' invention.

As none of the cited prior art, individually or in combination, disclose or suggest all the elements of independent Claim 1, Applicants submit the inventions defined by Claim 1, and all claims depending therefrom, are not rendered obvious by the asserted prior art for at least the reasons stated above.<sup>5</sup> Applicants submit the inventions recited in independent Claims 15, 28, 33, 34, 46, and 47 for substantially similar reasons.

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<sup>5</sup> MPEP § 2142 "...the prior art reference (or references when combined) must teach or suggest **all** the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

Accordingly, in view of the present amendment and in light of the previous discussion, Applicants respectfully submit that the present application is in condition for allowance and respectfully request an early and favorable action to that effect.

Respectfully submitted,

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